AMENDMENTS TO THE SPECIFICATION

IN THE TITLE:

Please replace the title of the invention with the following amended title:

SUBSTRATE FOR BIOMOLECULE MICROARRAY, BIOMOLECULE MICROARRAY, DEVICE AND METHOD ~~FOR INTERACTION ACCELERATION, AND INTERACTION DETECTING METHOD~~OF PROMOTING INTERACTION, AND METHOD OF DETECTING INTERACTION

IN THE SPECIFICATION:

Please replace the paragraph beginning at page 7, line 30 with the following amended paragraph:

~~Fig. 13~~Fig. 14 is an example of a substrate that can be used in the method of making interaction between biomolecules of the present invention.

Please replace the paragraph beginning at page 7, line 32 with the following amended paragraph:

~~Fig. 14~~Fig. 13 is a graph showing the intensity of the hybridization signal obtained in Example 5.

Please replace the paragraph beginning at page 16, line 2 with the following amended paragraph:

The ~~nucleic acid~~ biomolecule microarray of the present invention is characterized by comprising the substrate of the present invention and a biomolecule; and in that the biomolecule

is immobilized on at least the flat surface for spotting on the substrate. The biomolecule can be at least one selected from the group consisting of DNA, RNA, PNA, protein, polypeptide, sugar compound, lipid, natural small molecule, and synthetic small molecule. It can be selected based on the objective.

Please replace the paragraph beginning at page 25, line 16 with the following amended paragraph:

The substrate employed in the above-mentioned method is one provided with at least a pair of electrodes on the same surface as the surface on which biomolecule-immobilized spots are provided so that the biomolecule-immobilized spots place between a pair of electrodes mentioned above. ~~Fig. 13~~ Fig. 14 shows an example of such a substrate. In the substrate of ~~Fig. 13~~Fig. 14, for example, a layer comprised of an electrically conductive substance is formed on a part of the substrate by photolithography or the like to form a pair of electrodes opposed each other. In this method, a biomolecule microarray prepared by immobilizing biomolecules on such a substrate can be employed. In this method, such a microarray is employed, a biomolecule microarray having biomolecule-immobilized spots and a solution comprising a target biomolecule are brought into contact between the electrodes, and an electric field is applied between the electrodes in a state where the target biomolecule solution contacts with the electrodes. In this manner, the target biomolecules are caused to migrate toward the biomolecule-immobilized spots by dielectrophoresis (when an alternating current power source is employed) or by electrophoresis (when a direct current power source is employed) to increase the concentration of the target biomolecules in the vicinity of the biomolecule-immobilized spots, thereby promoting interaction between the biomolecules. In particular, in the present invention, interaction between the biomolecules can be markedly promoted by incorporating into the target biomolecule solution at least one buffer substance selected from the group consisting of phenylalanine, histidine, carnosine and arginine, particularly phenylalanine, having the markedly high effect in promoting interaction between biomolecules with the application of an electric field. The electric field that is applied between the electrodes can be suitably set based

on the type of buffer substance employed within a range permitting concentrating of the target biomolecules by electrophoresis or dielectrophoresis. For example, it can be set within a range of 0.5 to 1.0 MV/m. For the above-stated reasons, the power source employed is desirably a high-frequency alternating current power source.

Please replace the paragraph beginning at page 30, line 3 with the following amended paragraph:

A probe DNA solution (1 x microspotting solution (Terechem Corp.), 0.1 percent Tween20) was stamped to a concentration of 180 μM with the high-density arrayer on a substrate prepared in Example 1. The stamped probe gene was ~~GADPH~~ GAPDH (5'-gcagtggcaa agtggagatt gttgccatca acgacccctt cattg-3'(Seq. ID No. 8)) that had been modified on the 5' end with array-use linker (Nisshinbo Industries,Inc.). Following stamping, the substrate was irradiated with 600 mJ/cm^2 of UV, washed twice for 5 minutes with ultrapure water, and dried. After preparing target DNA solutions (1 μM 5' terminal Cy3 fluorescent oligo DNA (a sequence complementary to the probe DNA), buffer containing 10 to 50 mM of phenylalanine, histidine, carnosine, or arginine), and the above-described array was placed on a thermal cycler set to 45°C. An insulating film 30 μm in thickness (Teijin DuPont film) was placed along the perimeter of the array as a spacer, and 20 μL of target DNA solution were applied to the stamped area. Next, a glass slide substrate (opposite electrode) coated with an indium tin oxide (ITO) film was placed over the top and the two substrates were secured (Fig. 6). A hybridization reaction was conducted while applying an electric field of 1 MHz, 0 to 50 Vp-p for 10 minutes between the microarray and the opposite electrode. Following the reaction, the array was washed and the hybridization signal intensity was calculated. The results are given in ~~Fig. 14~~Fig. 13. (a) is a graph showing the correlation between the electric field applied and hybridization signal intensity, and (b) is a graph of the intensity ratio (referred to hereinafter as the "rate of signal increase") to the signal obtained when hybridization was conducted without applying an electric field. Table 1 shows the results for the electric field producing the greatest rate of signal increase for each buffer. As shown in Table 1, compared to hybridization without an electric

field, phenylalanine produced a hybridization increase rate of 6.54-fold with an electric field of 0.8M Vp-p/m; L-histidine, 3.66-fold with an electric field of 0.78M Vp-p/m; carnosine, 2.16-fold with an electric field of 0.53M Vp-p/m; and L-arginine, 2.66-fold with an electric field of 0.25M Vp-p/m ~~(Fig. 3-1, 2; the figure numbers will be changed later)~~. These results reveal that when buffers containing phenylalanine, histidine, carnosine, and arginine were employed, particularly when phenylalanine was employed, the method of promoting interaction between biomolecules of the present invention produced a good hybridization promoting effect.

AMENDMENTS TO THE SEQUENCE LISTING

Please replace the Sequence Listing of record with the substitute Sequence Listing enclosed herewith.